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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,380	04/01/2002	Fabrizio Samaritani	P/42-63	7114

7590 11/01/2005

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EXAMINER	
DEBERRY, REGINA M	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,380	SAMARITANI ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

Applicant's arguments have been entered in full (10 August 2005). Claims 1-15 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 1-3, 6-10, 13-15 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Maa *et al.,* US Patent No. 6,284,282 B1. The basis for this rejection is set forth at pages 3-5 of the previous Office Action (10 February 2005).

Applicant discusses the instant invention. Applicant contends that certain amino acids at specific positions in GRF require stabilization. Applicant argues that there is no teaching or suggestion in the cited references or in the application background suggesting the use of saccharose as a stabilizer. Applicant argues that Maa is concerned with the general method rather than stabilizing any particular therapeutic protein. Applicant argues that among the 34 specific proteins mentioned is GRF, although this is not one of the preferred proteins. Applicant cites case law. Applicant contends that a person skilled in the art, if motivated to try, would spend untold hours of experimentation to test every excipient listed by Maa in varying amounts before having the possibility of arriving at a stabilizing amount of saccharose as used in the present

invention. Applicant argues that it is significant that Maa lists mannitol as a possible excipient in that mannitol was known in the art, prior to the present invention, to be the best stabilizer for GRF. Applicant submits that the fact that saccharose provides a stability, which is better than mannitol is surprising and unexpected.

Applicant's arguments have been fully considered but are not deemed persuasive. The disclosure and claims of an issued patent are presumed to be fully enabled. The instant claims are drawn to GRF and saccharose, alone or in combination with other excipients. Maa *et al.* clearly teach that a composition comprising GRF may contain excipients, which ensure or increase the stability of the protein. Maa *et al.* list sucrose (i.e. saccharose) as one of the excipients.

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claims 1, 4, 5, 11 and 12 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Maa *et al.,* US Patent No. 6,284,282 B1 as applied to claim 1 and further in view of Samaritani, WO 95/35116 and Fujioka *et al.,* US Patent No. 4,963,529. The basis for this rejection is set forth at pages 4-5 of the previous Office Action (10 February 2005).

Applicant argues that the Samaritani reference is explicitly limited to human growth hormone (HGH) and that GRF is very different from HGH. Applicant discusses the amino acids in GRF. Applicant contends that no attempt has been made to establish that HGH has these amino acids at these positions and therefore, there is no factual

basis in the record for contending saccharose will stabilize anything other than HGH. Applicant cites case law. Applicant argues that saccharose may stabilize HGH does not suggest it will stabilize GRF.

Applicant discusses the Fujioki reference. Applicant argues that there is no teaching or suggesting in the reference that saccharose can be used as an effective stabilizer for GRF and that the reference implies that finding an effective stabilizer for GRF is difficult. Applicant submits that the instant specification teaches that the peptide purity of GRF/mannitol compositions decreased by about 2% over the 4-week study whereas the GRF/saccharose containing formulation decreased by 0.2% over the same period of time. Applicant contends that saccharose provided a stability which is better than mannitol, which is surprising and unexpected when viewed in light of the conclusion in the Office Action that GRF or GRF plus mannitol would be expected to behave in the same manner as with saccharose.

Applicant's arguments have been fully considered but are not deemed persuasive. Maa *et al.* teach a composition comprising GRF and saccharose. The MPEP 2143 states (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The Examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation

to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the GRF and saccharose pharmaceutical composition of Maa *et al.,* by formulating it with 68.4 mg/vial of saccharose as taught by Samaritini or a 10 mg/vial of hGRF, as taught by Fujioka *et al.,* with a reasonable expectation of success. The motivation is provided by the fact that adjustments of conventional working conditions such as protein and excipient concentrations are deemed a matter of judicious selection and routine optimization, which is well within the purview of the skilled artisan. Samaritani teaches 68.4 mg/vial of saccharose (page 6, lines 5-14). Samaritani teaches that highly purified proteins are stabilized with saccharose and that saccharose prevents the formation of a precipitate when the reconstituted solutions are shaken (page 1, lines 4-8 and page 4, lines 13-16). Fujioka *et al.* teach 10mgs/vial of GRF (column 3, lines 25-55).

Lastly, the Examiner stated that no art of record had been provided, which teach that saccharose would denature or destabilize GRF. Thus, there is no evidence that GRF would be expected to behave differently in saccharose (i.e. destabilize). The specification does not demonstrate that the stability results were greater than those that would have been expected from the prior art to an unobvious extent. There are no

unexpected results or properties because saccharose is a known stabilizer. Most importantly, Maa *et al.* teaches compositions comprising GRF and saccharose.

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RMD
10/28/05

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